THE RELATION BETWEEN SPATIAL NAVIGATION AND ASSOCIATIVE MEMORY IN THE OLDER ADULT POPULATION

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THE RELATION BETWEEN SPATIAL NAVIGATION AND ASSOCIATIVE MEMORY IN THE OLDER ADULT POPULATION

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LIST OF ABBREVIATIONS

MRI: magnetic resonance imaging

MOCA: Montreal Cognitive Assessment

MAS: Memory Assessment Scales

YA: younger adults

OA: older adults

CN: caudate nucleus

AD: Alzheimer’s disease

VMLT: Virtual Maze Learning Task

MCI: mild cognitive impairment

SPM: Statistical Parametric Mapping

DARTEL: Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra

MNI: Montreal Neurological Institute

MarsBaR: MARSeille Boîte À Région d’Intérêt

SUMMARY

Navigation strategy and spatial navigation aim to explain how humans engage with the world around them. They are also both a way to understand cognitive differences between age populations. Associative memory is the ability to learn and remember unrelated ideas. The purpose of this study is to determine the relationship between spatial navigation and associative memory in the older adult population. Part of the study includes using volumetric data from structural MRI to analyze spatial navigation abilities and memory performance. This study consists of twenty previously screened older adult subjects. The subjects then go through a series of tasks: the Associative Memory Task, the Route Learning Maze, the Y-Maze, and the Recognition tasks, as well as two neuropsychological assessments (MOCA and MAS). Data collected from these tasks are then analyzed, along with the subjects' structural MRI data from previous years. The major findings of this experiment were that landmark recognition correlates with directional association for critical landmarks, allocentric navigation preference yields higher associative memory performance, and an increase in hippocampal volume correlates with directional association and associative memory. Implications of this study may help identify navigational deficits and associative memory deficiencies in neurodegenerative diseases such as Alzheimer's disease, and these implications may lead to the identification of key neural markers for the discovery of potential therapies.

CHAPTER 1

INTRODUCTION

Spatial navigation plays an important role in the everyday lives of human beings. This complex cognitive skill aids in daily functioning [6]. It is best described as how one moves through space. Associative memory is the ability to learn and remember the relationship between unrelated objects or concepts [16]. This skill is particularly useful—without associative memory, it would be impossible to remember faces or places. The exact relationship between spatial navigation and associative memory is not fully known, but proficiency in these two areas vary with age.

In addition, the young adult population (YA) and the older adult population (OA) are known to have different navigation strategies in virtual environments, either egocentric or allocentric. The egocentric strategy, also called the response strategy, is self-referential, meaning the individual navigates based on a self-centered frame of reference. In contrast, the allocentric strategy, also called the place strategy, is self-external, meaning the individual navigates using their surroundings and landmarks [13]. The YA population is equally distributed between using egocentric and allocentric strategies, while the OA population uses solely the egocentric strategy [13].

There have been previous studies that related strategy choice to associative memory, but these results were varied. In one study, navigation by allocentric strategy yielded a higher performance on associative memory tasks than navigation by egocentric strategy [1]; however, not all the studies produced these same results [18][19]. Another study concluded that the allocentric navigation strategy yielded higher performance on associative memory tasks but solely for object-location associative memory tasks [11]. These studies suggest that the shift to a more egocentric strategy may relate to performance on associative memory tasks, but this shift in strategy has only been recently explored and is not well understood. More research must be done on the older adult population to determine the exact relationship between spatial navigation and associative memory performance. The objective of this research is to determine this relationship between the two in the older adult population. The primary hypothesis of this experiment is that the more egocentric the navigation strategy, the worse the associative memory performance is. Through the use of associative memory tasks, navigation through virtual environments, and analysis of structural MRI volumes, the relationship between spatial navigation and associative memory in the older adult population was assessed. This research will add to its field by determining how aging affects the covariance of navigational ability and associative memory, as well as assessing how navigation strategy in virtual environments changes across age groups.

CHAPTER 2

LITERATURE REVIEW

2.1 Spatial Navigation

Spatial navigation is an important cognitive skill that is used by animals every day to aid in their proper function [6]. It is best described as how one moves through space. In the current body of research, spatial navigation performance and strategy are known to vary with age.

2.1.1 Regions of interest

Research has shown that spatial navigation correlates with certain areas of the brain. In an experiment by Moffat *et al.*, the researchers wanted to know whether there was any relationship between spatial navigation and certain areas of the brain, specifically the hippocampal and extrahippocampal regions. Younger adults and older adults navigated through a virtual environment while in an MRI machine, and their brain volumes in specific regions taken from the resulting images were compared. These regions were the caudate nucleus, cerebellum, hippocampus, prefrontal, and primary visual cortices. It was found that successful spatial navigation employs both the hippocampal and extrahippocampal regions [8]. A larger CN and prefrontal gray and white matter correlated with better spatial navigation in the virtual environment. Younger adults were shown to have a larger hippocampus, and this was linked to a better performance overall.

In another study, researchers used functional MRI instead of structural MRI to determine how functional brain activation changes with age as a subject navigates through a virtual environment. With similar methods as the previously mentioned study, it was found that in the same areas of the brain, older adults had reduced activation compared to younger adults, except for in the anterior cingulate gyrus and medial frontal lobe, where older adults showed a higher activation than younger adults [7]. The cognitive process of spatial navigation used age-specific neural networks, and it was determined that the specific areas of the brain that elicit age differences in spatial navigational skill and memory can be identified.

2.1.2 Virtual Maze Method

Spatial navigation ability can be measured in several ways, but one of the most common and most reliable ways to quantify navigation ability and strategy is by using a virtual environment. This is a computer-generated environment that takes the form of any type of maze (Y-maze, Morris water maze, or generic route learning maze). In a previous study, researchers wanted to determine how using a virtual environment as a test for cognitive aging would compare to other tests to measure cognitive function as it varies with age [9]. A spatial navigation task in the form of a maze with textured walls, dead ends, and a goal at the end was used for the study. Based on the results of the study, the virtual maze method was found to successfully measure spatial navigation performance and route learning ability [9].

2.2 Associative Memory

Associative memory is the ability to learn and remember the relationship between unrelated objects or concepts [16]. Studying associative memory is important for research in the neurological field of medicine. Memory loss is often the first and most prominent symptom of Alzheimer's disease (AD), which is characterized by an impaired form of associative memory and recollection [2]. Previous studies show that this deficit in associative memory is due to anatomical changes in areas of the medial temporal lobe, including the hippocampus [5].

2.3 Effects of Age on Spatial Navigation

Literature in the field shows that aging has an effect on spatial navigation in terms of ability and navigation strategy [9][8][14].

2.3.1 Ability

In a study to determine the relationship between age and spatial navigation ability, it was found that older adult subjects performed worse on the spatial navigation task in all aspects – they took a longer time to complete the maze and traveled more distance, which, in turn, gave a higher frequency of hitting dead ends [9]. A higher percentage of younger adults compared to older adults were able to complete the maze without making any errors, i.e. hitting any dead ends. It was concluded that spatial navigation performance and the subject's ability to perform mental rotation, as well as their visual and verbal memory, have a positive correlation.

2.3.2 Navigation Strategy

In another experiment, the effect of age on preference for navigation strategy in a virtual environment was determined. It is known that older animals prefer the egocentric place strategy, and younger animals usually prefer the allocentric strategy. The experiment tested a group of young adults and a group of older adults using a virtual Y-maze, a virtual Morris water maze, and a cognitive mapping assessment. The results of the experiment showed that there are differences in place strategy preference in humans due to age – older adults prefer the egocentric place strategy, while younger adults chose both the egocentric and allocentric place strategy [14]. These findings are very important, since they demonstrated that there are age differences in spatial navigation strategies.

People who use the place strategy, also called place learners, rely on a frame of reference external to the individual, based on using a cognitive map with external reference points. This strategy is also known as self-external, or the allocentric strategy [13]. On the other hand, individuals who employ the response strategy, also called response learners, remember directions or a route based on a frame of reference centered on himself or herself, independent of an absolute position. This strategy is also known as self-referential, or the egocentric strategy [13]. The utilization of survey knowledge for place learners and procedural stimulus-response learning for response learners is controlled by the hippocampus and caudate, respectively [1][4][12][15].

2.4 Effects of Age on Associative Memory

Early studies assessed age-related deficits in navigational ability. These studies showed that "non-demented elderly adults are less proficient than younger adults at learning novel routes…and associating landmarks to specific locations or places"

[17][9][10][3]. However, with research having been done on age-related deficits in navigational ability, further examination into age-related differences in associative learning was still needed. Another study explored these differences with regard to the associative learning of landmarks and heading directions during route navigation [20].

This study focused on associative memory and how it relates to an individual's performance in landmark recognition and landmark-directional association. In this study, participants of all age categories (young adults, middle-age adults, older adults) were assessed for their differences in route learning abilities and memory task performance after having navigated through a virtual maze with critical and non-critical landmarks [20]. Critical landmarks were those located at intersections, or decision points. Non-critical landmarks were those located on the sides of the maze; these are non-decision points [20].

The researchers found that older adults have more navigation errors than younger adults during route learning. In addition, older adults were found to be poorer at critical and non-critical landmark-direction associative learning, especially at decision points. Furthermore, older adults regarded non-critical landmarks as "distractors" or "irrelevant cues." From these results, it can be predicted that older adults "may expend more cognitive resources on the encoding of landmark/object features than on the binding of landmark and directional information" [20].

2.5 Navigation Strategy and Associative Memory

Some research has been done regarding the relation between navigation strategy and associative memory; however, not much is known about this relationship other than that the hippocampus is involved in both neural processes. In a study conducted by Bohbot et al., it was found that navigation by place strategy, which is controlled by the hippocampus, yields better performance on associative memory tasks than navigation by response strategy, which is controlled by the caudate [1]. However, not all research supports this theory [18][19]. Recently published work by Ngo et al. on non-expert young adults found that “preference for a place strategy positively correlated with spatial (object-location) associative memory performance but did not correlate with non-spatial (face-name) associative memory performance” [11]. They concluded that preference for the allocentric spatial navigation strategy only spatially correlated with associative memory, which indicates that the connection between spatial navigation strategy and associative memory is only for spatial performance.

CHAPTER 3

MATERIALS AND METHODS

3.1 Pre-Experiment

Older adults (age 60-80 years) were screened over the phone using a Health Phone Questionnaire. If the subject was found to be eligible for the study, the subject was then scheduled to be tested. The study was counterbalanced for each subject, so each subject performed the tasks in a different order. This was done to avoid any possible confounding variables that may have occurred due to a specific order of tasks given; e.g. a subject may perform better on tasks given first since they are not as tired. Twenty OA subjects were used in this study.

3.2 Associative Memory Task

There were two parts to the Associative Memory Task, an Encoding portion and a Retrieval portion. In the Encoding task, the subject was shown pictures of objects and backgrounds. The subject must indicate if the object in the background is “common” and “pleasant.” In the Retrieval task, the subject was shown pictures of objects. The subject must determine if the pictures are from objects shown in the Encoding task, or if the objects shown are new objects. If the objects are denoted as “Old,” meaning the subject has seen them before in the Encoding task, then they are asked to match the picture of the object to the background it was on during the Encoding task.

3.3 Spatial Tasks

There were two spatial tasks in the form of mazes that the subject had to complete, the Y-Maze and the Route Learning Maze. The Y-Maze is a virtual maze with a predetermined goal. There are five consecutive trials to determine goal location. The Route Learning Maze, also known as the virtual maze learning task (VMLT), had the subject navigate through the maze to find the end.

3.3.1 Y-Maze

This task determined the subject's pre-existing preferences for allocentric vs. egocentric strategy use. It is a Y-shaped maze in a room with visual cues. There are 5 blocks, with two parts each: training and probe. To move on to the probe trial, the subject must reach the goal area for five consecutive successful trials. The correct goal was indicated with pleasing tone; the incorrect goal was indicated with a buzzer sound. In the probe trial, the subject was allowed to move to whichever goal, and no sound was given. The probe trial was designed to determine allocentric or egocentric strategy preference.

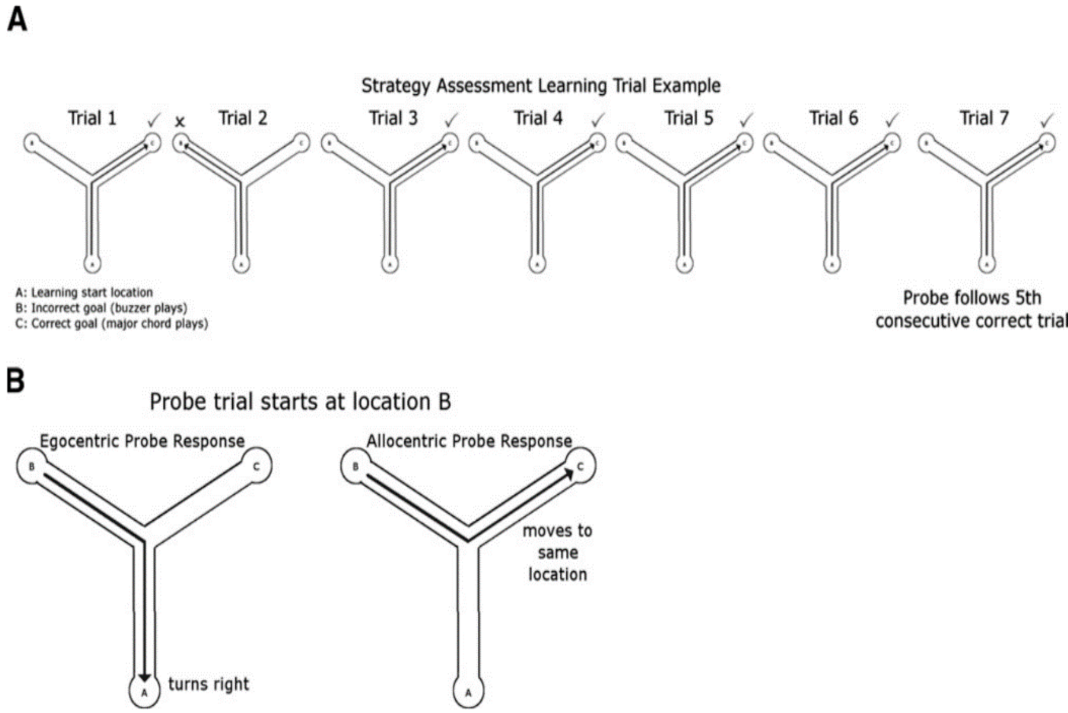

Figure 1. Y-Maze. This task will determine subject's pre-existing preferences for allocentric vs. egocentric strategy use. It is a Y-shaped maze in a room with visual cues. There are 5 blocks, with two parts each: training and probe. To move on to the probe trial, subject must reach goal area for five consecutive successful trials. Correct goal is indicated with pleasing tone; incorrect goal is indicated with a buzzer sound. In the probe trial, the subject is allowed to move to whichever goal, and no sound is given. The probe trial is designed to determine allocentric or egocentric strategy preference.

3.3.2 Virtual Maze Learning Task

This task was in the first-person perspective and comprised of alleys and intersections. The subject decided which alley to take in each intersection; only one direction in the intersection choices led to the finishing point, with the others leading to a dead end. Landmarks in the form of wall pictures facilitated maze learning.

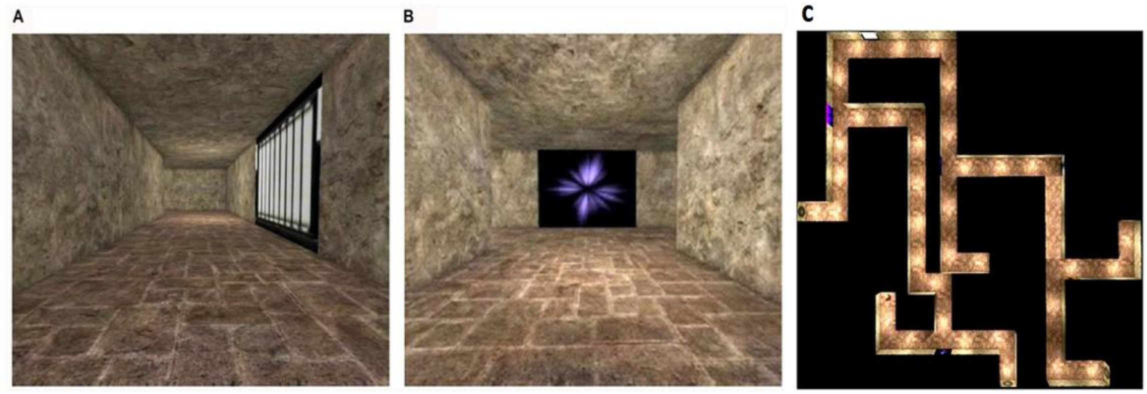

Figure 2. Virtual Maze Learning Task. This task is in first-person perspective; comprised of alleys and intersections. Participant decides which alley to take in each intersection; only one in the intersection choices lead to the finish point with the others leading to a dead end. Landmarks in the form of wall pictures facilitate maze learning.

3.4 Recognition Tasks

There was one follow-up task to the Y-Maze, and two follow-up tasks to the Route Learning Maze. In the Y-Maze Recognition Test, the subjects were given pictures of objects, and they must determine which objects were used in the Y-Maze assessment. In the Spatial Navigation Recognition Test, the subjects were given pictures of objects, and they must determine which objects were used in the Route Learning Maze. In the Directional Association Test, the subjects were given screenshots of the Route Learning Maze, and they must determine which direction to travel.

3.5 Neuropsychological Tests

The subjects were administered two neuropsychological tests to assess normative memory and cognitive functions: the Montreal Cognitive Assessment (MoCA) and the Memory Assessment Scales (MAS) test.

3.6 Analysis

The results from the behavioral data and the structural MRI brain scans were analyzed. Behavioral data included the Associative Memory Task, Y-Maze Task, Virtual Maze Learning Task, and Recognition Tasks. MOCA and MAS scores were graded to ensure that the subjects did not have mild cognitive impairment (MCI) or unusually low memory performance that would deviate from general population norms.

3.6.1 Behavioral data

Memory performance and spatial navigation performance were analyzed for each of the twenty subjects in the study.

For the Y-Maze trials, a score of 0 was assigned to an egocentric navigation strategy, and a score of 1 was assigned to an allocentric navigation strategy. This gave a range of scores from 0-5. If the score for the subject was less than or equal to 2, they were said to have a preference for the egocentric navigation strategy. If the score for the subject was greater than or equal to 3, they were said to have a preference for the allocentric strategy.

For the Virtual Maze Learning Task, a score was given for each intersection in the maze. Each intersection comprised of a straight path, a left path, and a right path. The score for the intersection was given based on the number of times it took to choose the correct heading direction (left, right, or straight). Data were also collected from the other computer tasks – Associative Memory Task and the Recognition tasks. Graphs were made from the analyses of experimental data.

3.6.2 Structural MRI

Structural MRI brain scans from the twenty OA subjects were used as another level of analysis for this study. These scans were the result of the subjects' participation in other studies from the Memory and Aging Lab where volumetric data was collected. To begin analysis, the SPM 12 program was used to run DARTEL. The Memory and Aging Lab protocol for running DARTEL using SPM 12 was followed.

The first step in DARTEL was to do a manual reorientation for the scans to optimize segmentation and normalization. Each subject's T1 image was adjusted to align with the SPM T1 templates. This adjustment is necessary because subjects are often tilted in the MRI scanner, and manually reorienting these scans will reduce errors in segmentation and normalization by aligning them with the MNI space. The second step was segmentation, in which roughly aligned grey and white matter images of the subjects are generated. The third step in DARTEL was creating the structural templates that are based on the specific data that was inputted into the program. The next step in this process was to normalize the MNI space, which produces a spatial transformation for the group data. In this step, files containing each subject's grey matter, white matter, and CSF were generated. Upon completion of DARTEL, a toolbox for SPM called MarsBaR was used for region of interest analysis. This allowed statistical analyses of ROI data to be performed using SPM.

CHAPTER 4

RESULTS

4.1 Landmark Recognition correlates with Directional Association only for Critical Landmarks

Subjects navigated through the Route Learning Maze, and upon completion, were administered two recognition tests: the Spatial Navigation Recognition Test and the Directional Association Test. The results from these tests were analyzed and graphed on a scatter plot. In the Spatial Navigation Recognition Test, subjects were given pictures of objects and had to determine which objects were used in the RLM. In the Directional Association Test, subjects were given screenshots of the RLM for both critical and non-critical intersections and had to determine in which direction to travel, using the pictures of objects on the walls of the maze as a guide. Critical intersections were defined as the 3-way intersections in the maze, where the subject could choose to maneuver left, right, or go straight. Recognition accuracy for critical intersections is represented as blue triangles in Figure 3. Non-critical intersections were defined as the hallways where the subject could only move in the straight direction, i.e. they were not required to decide in which direction to travel. Recognition accuracy for non-critical intersections is represented as green circles in Figure 3.

The horizontal axis of this graph shows average landmark recognition accuracy. Landmark recognition is the ability to correctly recognize whether the objects in the pictures (landmarks) on the wall of the RLM were actually seen during the RLM task. The vertical axis of this graph shows the directional association accuracy. Directional association is the ability to choose the correct direction when shown an intersection with multiple options. $R^2 = 0.13$ for critical intersections. $R^2 = 0.001$ for non-critical intersections. The correlation coefficient, which is a numerical measure of correlation representing the linear dependence of two variables, was found to be 0.23 for landmark recognition and directional association.

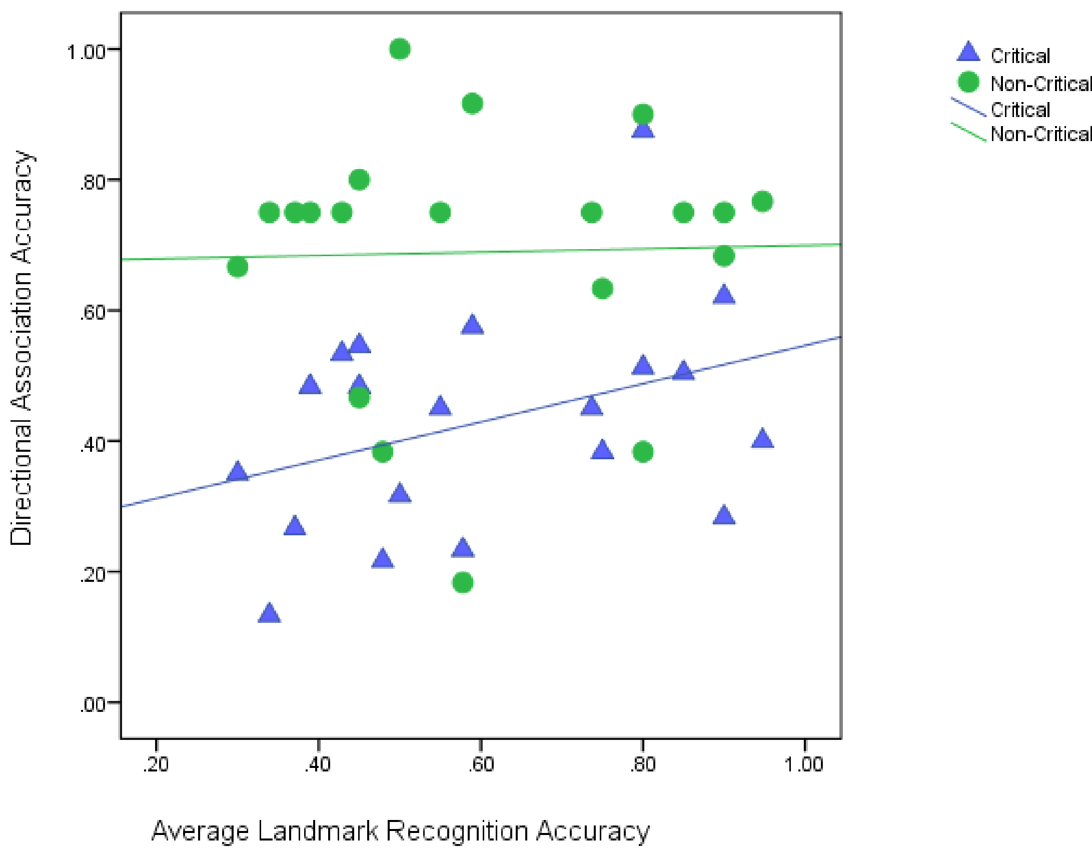

Figure 3. Landmark Recognition correlates with Directional Association only for Critical Landmarks. Subjects were administered recognition tests upon completion of the Route Learning Maze. Data resulting from Spatial Navigation Recognition Test and Directional Association Test were analyzed and plotted on scatter plot. In the Spatial Navigation Recognition Test, subjects were given pictures of objects and had to determine which objects were used in the RLM. In the Directional Association Test, subjects were given screenshots of the RLM for both critical and non-critical intersections and had to determine in which direction to travel, using the pictures of objects on the walls of the maze as a guide. $R^2 = 0.13$ (critical) and 0.001 (non-critical). Correlation coefficient was found to be 0.23.

4.2 Allocentric Navigation Preference yields higher Associative Memory Performance

Figure 4 shows a scatter plot with a line of best fit ($R^2 = 0.201$). The y-axis shows the average source memory performance, or associative memory. Source memory accuracy is the subject's performance on the Associative Memory Task—i.e., how well they remembered the background paired with the objects. The x-axis shows the total score for each subject across the five trials. Across the five maze trials, an egocentric strategy was given a score of 0, and an allocentric strategy was given a score of 1. This made the range of possible scores across the five maze trials 0-5. A subject with a score of 2 or less is said to have a preference for the egocentric navigation strategy, and a subject with a score of 3 or greater is said to have a preference for the allocentric navigation strategy. The graph shows that when the subject prefers the allocentric navigation strategy, they have better associative memory performance. The graph can also be viewed as showing that the more egocentric the navigation strategy becomes, the lower the associative memory performance will be. Associative memory and navigation strategy have a correlation coefficient of 0.45 ($p < 0.01$).

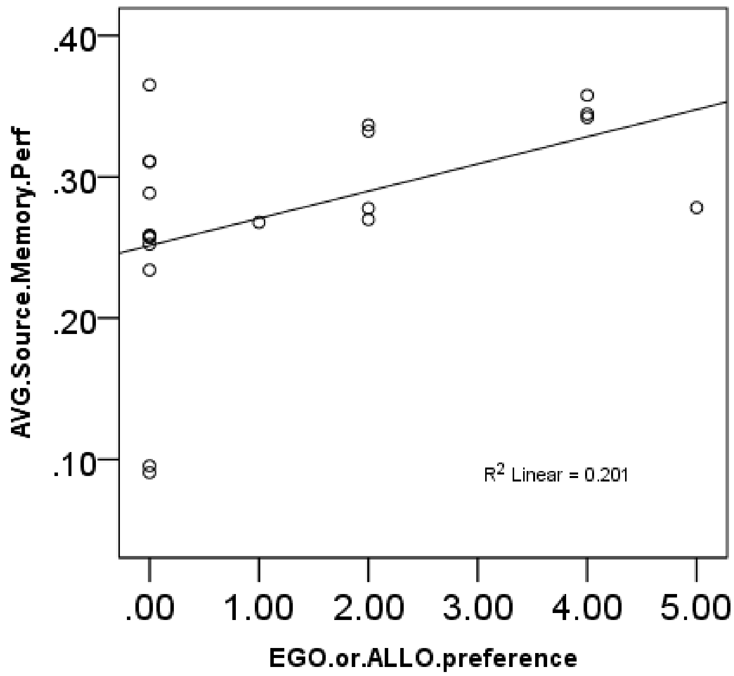

Figure 4. Allocentric Navigation Preference yields a higher Associative Memory Performance. Data resulting from Y-Maze Task and Associative Memory Task were analyzed and plotted on the scatter plot. Across the five maze trials of the Y-Maze, egocentric strategy was given a score of 0; allocentric strategy was given a score of 1, for a maximum possible total score of 5. A subject with a score of 2 or less employs an egocentric strategy, and a subject with a score of 3 or greater employs the allocentric strategy. $R^2 = 0.201$. Correlation coefficient was found to be 0.45 ($p < 0.01$).

4.3 Greater Hippocampal volume correlates with Directional Association

The scatter plots in Figure 5 show the relationship between hippocampal volume and directional association at critical and non-critical intersections. The vertical axis shows the proportion of correct directional association, and the horizontal axis shows the hippocampal volume, controlling for total intercranial volume for each subject. Hippocampal volume was measured from the structural MRI scans of the subjects. The graph shows that as hippocampal volume increased, directional association at critical intersections increased, as well ($R^2 = 0.324$). Critical intersections are the three-way intersections in the Route Learning Maze where a decision must be made to determine which direction to travel (forward, right, left). However, as hippocampal volume increased, directional association at non-critical intersections decreased ($R^2 = 0.042$). These non-critical intersections are straight paths in the Route Learning Maze.

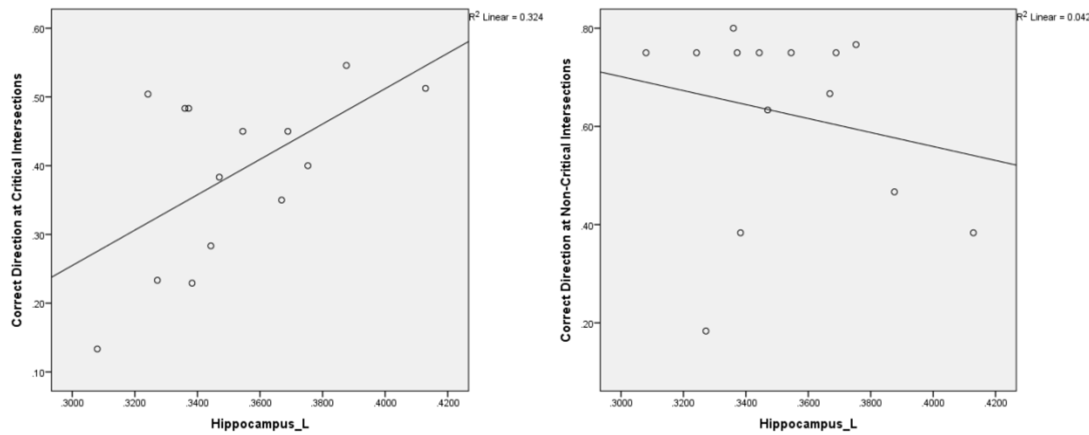

Figure 5. Greater Hippocampal volume correlates with Directional Association. Structural MRI volumes in the hippocampus were measured and analyzed in relation to directional association and plotted on a scatter plot. $R^2 = 0.324$ (critical), 0.042 (non-critical).

4.4 Greater Hippocampal volume correlates with Associative Memory

The scatter plots in Figure 6 show the relationship between hippocampal volume and associative memory. The vertical axis represents associative memory, and the horizontal axis represents hippocampal volume, controlling for total intercranial volume for each subject. Hippocampal volume was measured from the structural MRI scans of the subjects. The graph shows that as hippocampal volume increased, associative memory performance increased, as well ($R^2 = 0.176$).

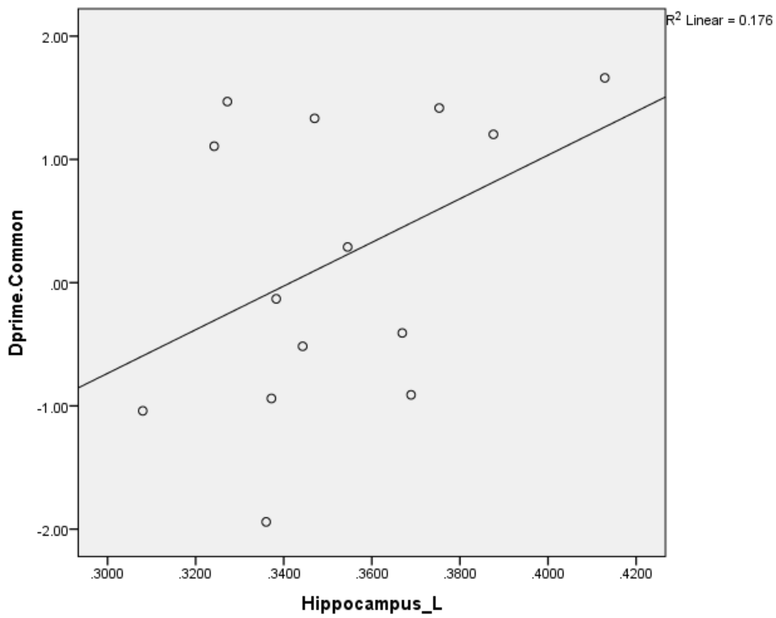

Figure 6. Greater Hippocampal volume correlates with Associative Memory. Structural MRI volumes in the hippocampus were measured and analyzed in relation to associative memory and plotted on a scatter plot. $R^2 = 0.176$.

CHAPTER 5

DISCUSSION

The results showed that landmark recognition correlates with directional association for only critical landmarks, and not non-critical landmarks. Previous literature has only found that older adults were poorer at non-critical and critical landmark-direction associative learning compared to younger adults; however, no research has been done until now that clearly defines the landmark-direction association in solely the older population [20]. The research from this experiment indicates that an older adult is more likely to recognize an object in a critical intersection than in a non-critical intersection.

Another finding in this study was that the allocentric navigation preference yields a higher associative memory performance. These findings support current literature in the field [1][11]. In addition, 16 of the 20 subjects in this study employed the egocentric navigation strategy, which also follows current literature findings [13][14]. These results support the hypothesis that the more egocentric the navigation strategy, the worse the associative memory performance is.

Previous research has shown that successful spatial navigation employs the hippocampal regions, which encouraged this study to focus on the changes in hippocampal volume and its correlation with directional association [8]. The results of this study found that an increase in hippocampal volume correlates with directional association. In addition, an increase in hippocampal volume also correlates with associative memory, which follows the current research trend [1]. This finding gives structural reasoning to the hypothesis of the study.

The shift in navigation strategy from allocentric to egocentric was not well understood, but this study helped add to the current body of research on this topic by investigating the relationship between spatial navigation and associative memory in the older adult population. This study determined how aging affects the covariance of navigational ability and associative memory, and how navigation strategy in virtual environments changes across age groups: Older adults were found to predominantly use the egocentric strategy, which was also shown to yield lower associative memory performance. This relationship between spatial navigation and associative memory was shown to change with age as well, since 80% of the older adult participants preferred the egocentric strategy, and younger adults mostly prefer the allocentric navigation strategy. The results of this study also found that more allocentric strategy results in higher associative memory performance. Therefore, as one ages, their navigation preference evolves from allocentric to egocentric, also decreasing their associative memory performance. In addition, an increase in hippocampal volume, which is utilized in spatial navigation, was found to correlate with higher associative memory performance.

Although this study produced significant findings regarding spatial navigation and associative memory, this research lacks definitive reasoning as to why this correlation exists. In other words, causation for this correlation between spatial navigation and associative memory needs to be explored in future studies.

CHAPTER 5

CONCLUSION AND FUTURE WORK

In conclusion, this work addresses gaps in the field of psychology and neuroscience by investigating the relationship between spatial navigation and associative memory in the older adult population. The effects of aging on navigation strategy are significant, and this research paves the way for a more in-depth comparison of the younger and older adult populations with regard to associative memory. Future studies may help identify navigational deficits and associative memory deficiencies in adults with Alzheimer's disease, which may lead to the identification of key neural markers for the discovery of potential therapies.

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